Global perceptions of the current and future impacts of COVID-19 on hereditary angioedema management

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ABSTRACT

Background: *The coronavirus disease 2019 (COVID-19) pandemic has greatly affected health-care provision across the globe. Management of chronic ailments has become challenging because of the strained health-care resources and social distancing measures that prevent on-site clinical visits and treatments. Hereditary angioedema (HAE) is a debilitating, chronic disease characterized by unpredictable swelling attacks in various parts of the body. Controlling HAE symptoms often requires long-term prophylactic medication use and regular medical care; however, limited scientific information has been published about HAE medical care during the COVID-19 pandemic.*

Objective: *To gather patient and health-care professional (HCP) perspectives on the global impact that COVID-19 has had, and the future impact it will have on HAE medical care and to identify differences in perceptions across economic and geographic boundaries.*

Methods: *We conducted two independent but similar online global surveys to capture patient and HCP perspectives on the impact that COVID-19 has had, and the future impact it will have on HAE medical care.*

Results: *Both patients and HCPs globally reported that the pandemic has limited the availability of HAE medical care, and they expect the restrictions to continue far beyond the pandemic. In addition, the results of our study suggested that telehealth use has increased across the globe but has been more successfully implemented in high-income countries.*

Conclusion: *Patients and HCPs expect that HAE-related care will be negatively impacted by the pandemic for many years. Disparities in medical care and technologic infrastructure may exacerbate these challenges in non–high-income countries. Supportive tools and global infrastructure should be established to provide aid to non–high-income countries throughout the pandemic and several years after.*

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The ongoing coronavirus disease 2019 (COVID-19) crisis continues to be a major global health emergency, with > 138 million confirmed cases and almost 3 million deaths worldwide (accurate as of April 21, 2021).[1,2] To reduce the spread of the virus, many countries have implemented preventative physical distancing measures, including public lockdowns and travel restrictions[3,4]; however, these measures have dramatically changed how the general population works, socializes, and performs daily tasks.[4,5] In addition, many countries have struggled to meet health-care demands in the past year because of the urgent need for hospital beds and emergency facilities. This demand has placed a strain on hospitals and health clinics, depleting resources necessary for maintaining normal health care processes.[5–7]

Furthermore, residents of non–high-income countries may face greater challenges during the COVID-19 pandemic because of inequalities in economic resources, access to technology, and vaccine availability.[5,6,8,9] For example, to achieve physical distancing standards and to compensate for limited medical resources, high-income countries have shifted the health-care paradigm toward the utilization of telehealth platforms.[8] Implementation of telehealth services has been less extensive in non–high-income countries, largely because of their more limited technologic infrastructure.[8] The diagnosis and treatment of patients with non–COVID-19-related illnesses has become more challenging in the wake of

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these health-care paradigm shifts.[7,10] For example, patients with chronic diseases require routine health-care visits, procedures, and treatments, which have all been greatly affected by the reduced health-care capacity in many countries.[7,10] Patients have missed medical treatments, endured extended durations between treatments, and discontinued treatments altogether.[10]

Hereditary angioedema (HAE) is a rare genetic disease characterized by recurrent, debilitating, and potentially lethal angioedema attacks in various parts of the body.[11,12] HAE attacks can be treated acutely with on-demand therapies to reduce the severity and duration of swelling episodes.[12] In addition, long-term prophylactic therapy can be used to reduce the frequency and severity of attacks.[13] Several HAE treatments can be self-administered at home, However, self-administration of parenteral treatments requires training and the availability of some medications is limited in many countries.[14,15]

As a chronic disease that necessitates frequent medical interventions, it is likely that HAE medical care has been greatly affected by the pandemic, but there are limited studies that describe how HAE medical care has changed or will change in the future because of the pandemic. Thus, we conducted two parallel surveys, one for patients with HAE and the other for health-care professionals (HCP) who treat patients with HAE, to better understand how the pandemic has affected HAE medical care globally and to determine differences in perceptions across geographic and/or economic boundaries. The results of these surveys are reported herein.

METHODS

Two separate, blinded, online surveys were conducted among two global respondent groups: patients with HAE and HCPs (physicians and nurses) who treat patients with HAE. The surveys were provided as a link on the HAE International web site[16] and on the HAE international Facebook page[17] as well as the personal Twitter and Facebook accounts of one of us (V.G.-P.) (the survey was open from October 4–24, 2020, with the social media links not established until October 9, 2020). All the responses were provided anonymously; however, the initial screener questions asked if the participant was a patient with HAE or an HCP who treated patients with HAE who were ≥ 18 years of age.

Both surveys were originally developed in English but were translated into 17 additional languages (listed in the Supplemental Material) to ensure the accuracy of responses across countries (all translations were performed by licensed court-certified translators). The surveys were approved by the institutional review board at the University Saints Cyril and Methodius, Skopje, North Macedonia (03–2943/2). Survey topics included basic demographics, HAE management before and during the COVID-19 pandemic, and prospects about future HAE management. Questions included multiple choice, Likert scale, and open-ended formats. Answer choices were developed based on the most frequently discussed topics and concerns expressed during national and international webinars throughout the pandemic. The patient respondents were asked 22 questions, and the HCP respondents were asked 25 questions.

All data were analyzed in aggregate. The means reported were unweighted. Comparisons were conducted across questions within the same respondent groups and between the country groups, which were defined by economic status. Country group 1 consisted of countries classified as high-income countries based on the World Bank group definition of economies with a gross national income per capita of $12,536 or more, as determined by the Atlas method.[18] Country group 2 consisted of countries classified as non–high-income countries based on the World Bank definition of economies with a gross national income per capita below $12,536, as determined by the Atlas method.[18] To assess the differences in the means between the groups, we used both parametric and nonparametric tests. In most cases, the distribution of the responses was approximately normal, and the two-sided *t*-test had superior power over nonparametric tests. However, the distributions were skewed in some cases, and a *t*-test may impose overly strong statistical assumptions. Because of this, we reported the results of both two-sided parametric *t*-tests and the results of a nonparametric Wilcoxon rank sum (Mann-Whitney two-sample) test. In all cases, we used a 5% significance level, and we reported a 95% confidence interval for the *t*-tests. Percentile values were rounded to the nearest 10th decimal.

RESULTS FROM THE GLOBAL PATIENT SURVEY

Patient Characteristics

Survey responses were collected from 135 patients who resided in 31 countries. Eighty-one patients resided in high-income countries (group 1), and 54 patients resided in non–high-income countries (group 2). Twenty-three percent of the patients were 18–30 years of age, 35.6% were 31–42 years of age, 28.9% were 43–54 years of age, and 12.6% were 55–73 years of age. The most common specialist types that patients reported consulting with about their HAE treatment were clinical immunologists (54.1%) and dermatologists/allergy specialists (28.2%);

Table 1 **Patient characteristics**

	Group 1 (n = 81)	Group 2 (n = 54)	Total (N = 135)
Age range, n (%)			
18–31 y	17 (20.1)	14 (25.6)	31 (23)
32–43 y	28 (34.6)	20 (27)	48 (35.6)
44–54 y	23 (28.4)	16 (29.6)	39 (28.9)
55–73 y	13 (16)	4 (7.4)	17 (12.6)
Country, n (%)			
Albania	0	1 (1.9)	1 (0.7)
Angola	0	1 (1.9)	1 (0.7)
Australia	1 (1.2)	0	1 (0.7)
Austria	1 (1.2)	0	1 (0.7)
Brazil	0	3 (5.6)	3 (2.2)
Canada	1 (1.2)	0	1 (0.7)
Croatia	4 (4.9)	0	4 (3.0)
Cyprus	1 (1.2)	0	1 (0.7)
Czech Republic	1 (1.2)	0	1 (0.7)
France	3 (3.7)	0	3 (2.2)
Germany	3 (3.7)	0	3 (2.2)
Greece	2 (2.5)	0	2 (1.5)
Israel	12 (14.8)	0	12 (8.9)
Italy	3 (3.7)	0	3 (2.2)
Mexico	0	1 (1.9)	1 (0.7)
Montenegro	0	1 (1.9)	1 (0.7)
Netherlands	1 (1.2)	0	1 (0.7)
North Macedonia	0	5 (9.3)	5 (3.7)
Poland	1 (1.2)	0	1 (0.7)
Portugal	1 (1.2)	0	1 (0.7)
Romania	31 (38.3)	0	31 (23.0)
Russia	0	1 (1.9)	1 (0.7)
Serbia	0	4 (7.4)	4 (3.0)
Slovak Republic	2 (2.5)	0	2 (1.5)
Slovenia	3 (3.7)	0	3 (2.2)
Spain	1 (1.2)	0	1 (0.7)
Sweden	2 (2.5)	0	2 (1.5)
Switzerland	1 (1.2)	0	1 (0.7)
Turkey	0	37 (68.5)	37 (27.4)
United Kingdom	1 (1.2)	0	1 (0.7)
United States	5 (6.2)		5 (3.7)
Specialist the patients reported consulting, n (%)			
General practitioner	4 (4.9)	3 (5.6)	7 (5.2)
Clinical immunologist	39 (48.2)	34 (63.0)	73 (54.1)
Pulmonologist	3 (3.7)	0	3 (2.2)
Otorhinolaryngology specialist	3 (3.7)	1 (1.9)	4 (3.0)
Dermatologist/allergy specialist	27 (33.3)	11 (20.4)	38 (28.2)
Gastroenterologist	0	1 (1.9)	1 (0.7)
Other	5 (6.2)	4 (7.4)	9 (6.7)

others reported consulting with general practitioners (5.2%), otorhinolaryngology specialists (3%), pulmonologists (2.2%), gastroenterologists (0.7%), and other (6.7%). Patient characteristics are reported in Table 1.

Perceived Impacts on Current and Future HAE Medical Care Due to the Pandemic

In total, 70% of the patients reported that the pandemic restricted their regular HAE medical care at least slightly, with an average rating of 2.6 of 5 on a

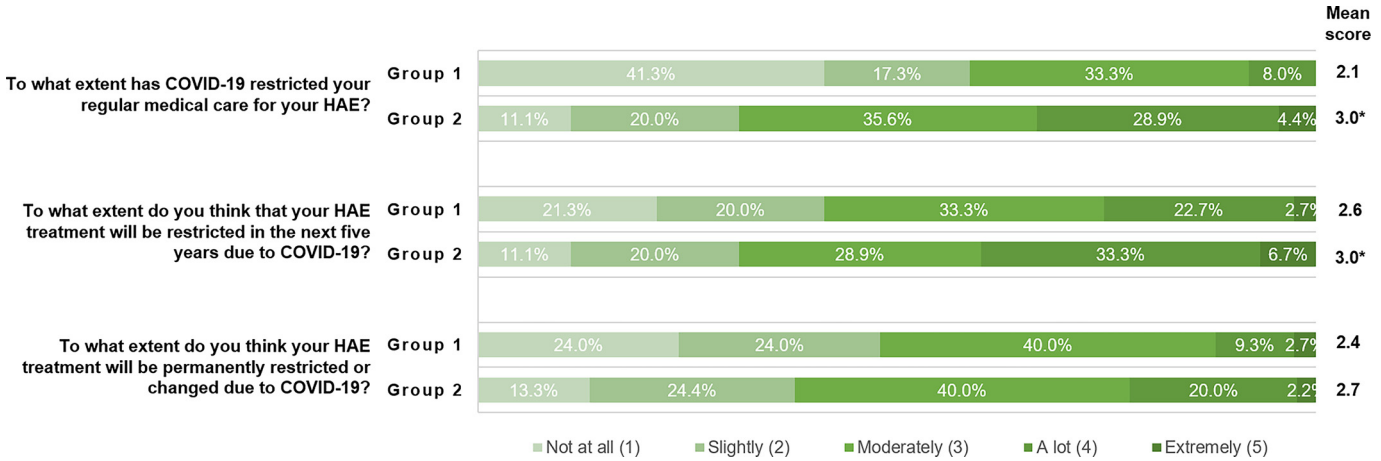

Figure 1. *Patient-perceived impact of the COVID-19 pandemic on HAE care and/or treatment. *p ≤ 0.05. COVID-19 = Coronavirus disease 2019; HAE = hereditary angioedema.*

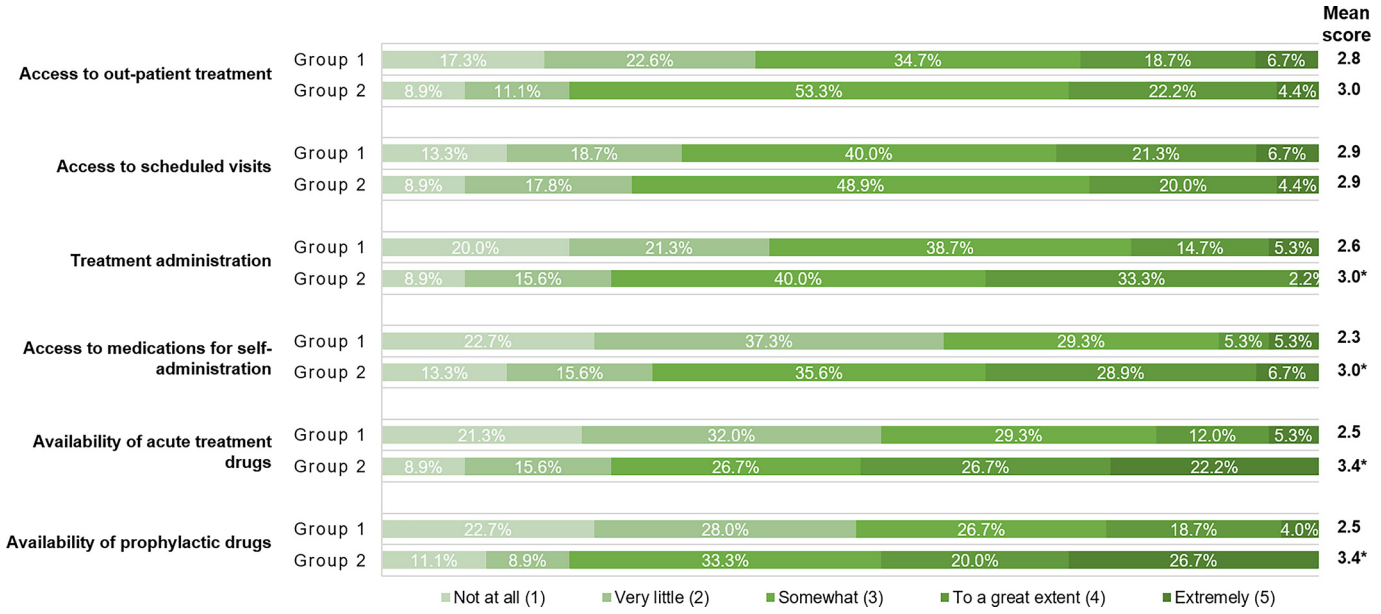

Figure 2. *Patient-perceived impact of the COVID-19 pandemic in the next 5 years on various aspects of HAE-related care and/or treatment. *p ≤ 0.05. COVID-19 = Coronavirus disease 2019; HAE = hereditary angioedema.*

scale from 1 to 5 (1 being not at all restricted and 5 being extremely restricted). On average, the patients in group 2 reported feeling that their HAE medical care was more restricted than did the patients in group 1 ($p < 0.001$, *t*-test and Wilcoxon rank sum test) (Fig. 1). Overall, 82.5% of the patients believed that the pandemic will restrict their regular HAE medical care at least slightly in the next 5 years, with an average rating of 2.8 of 5. On average, the patients in group 2 believed that they will experience a greater extent of future restrictions to HAE medical care in the next 5 years than did the patients in group 1 ($p = 0.07$, a *t*-test and Wilcoxon rank sum test) (Fig. 1). Also, 80% of the patients believed that the pandemic will permanently restrict or change their HAE medical care at least slightly, with an average rating of 2.5 of 5 (no significant difference between the groups) (Fig. 1).

On average, on a scale from 1 to 5 (1 being not at all affected and 5 being extremely affected), the patients in group 2 believed that several aspects of their HAE medical care will be more greatly affected in the next 5 years compared with the patients in group 1. Such aspects include the following: treatment administration ($p = 0.04$, *t*-test; $p = 0.03$, Wilcoxon rank sum test); access to medications for self-administration ($p = 0.001$, both tests); availability of acute treatment drugs ($p < 0.001$, both tests); and availability of prophylactic drugs ($p < 0.001$, both tests) (Fig. 2). The patients in group 1 believed that access to scheduled visits is the most likely aspect of their medical care to be affected

in the long term by the pandemic (mean score, 2.9), and the patients in group 2 believed that availability of prophylactic drugs is the most likely aspect of their care to be affected in the long term (Fig. 2). In addition, many patients reported being less satisfied with their HAE care during the pandemic compared with their care before the pandemic. Overall, 49.2% reported satisfaction with their current care versus 67.5% who reported satisfaction with their care before the pandemic (mean, 3.5 versus 3.8 on a scale from 1 to 5, with 1 being very dissatisfied and 5 being very satisfied) ($p = 0.01$, both tests; no significant difference between the country groups).

Satisfaction with Telehealth for HAE Management

Most patients (64.2%) agreed that face-to-face consultations for HAE management are important, with an average score of 3.6 on a scale from 1 to 5 (1 being not important and 5 being very important); the patients in group 2 rated face-to-face consultations as more important versus the patients in group 1 (mean, 4.0 versus 3.4; $p = 0.01$, t-test; and $p = 0.03$, Wilcoxon rank sum test). Despite these preferences, 92.5% of the patients reported that remote care visits and/or consultations are at least moderately useful, rating them an average 3.8 of 5, on a scale from 1 to 5 (1 being not useful at all and 5 being very useful). On average, the patients in group 1 rated the usefulness of remote care visits higher than the patients in group 2 (4.0 and 3.3, respectively; $p < 0.001$, both tests).

Unmet Needs

The patients were asked the following: "If you could give one piece of advice as a patient to health care professionals regarding treatment of HAE in the post COVID-19 era, what would you say?" The patients could choose one of the following options (results are included in parentheses after each option): "Help patients to clearly identify the symptoms of HAE through improved HCP-patient communications" (30.8%); "Regularly check the status of your patients, even if they aren't asking for a consultation" (25%); "Educate patients to more accurately assess whether they do or do not need to see their HCP" (24.2%); "Improve response time when patients report symptoms that may appear ambiguous or unclear" (15.8%); and "Other" (2.5%).

Patients with a COVID-19 Diagnosis

A total of seven patients surveyed (five from group 1 and two from group 2) had previously been diagnosed with COVID-19. All cases were reported as mild and did not affect the frequency or severity of the patients' HAE attacks. Only one patient (group 2) of the seven had received prophylactic HAE medication before the COVID-19 diagnosis.

RESULTS FROM THE GLOBAL HCP SURVEY

HCP Characteristics

Sixty-one HCPs responded to the survey with 37 residing in group 1 countries (high income) and 24 residing in group 2 countries (non–high income). The most common specialties included allergy (37.7%), clinical immunology (21.3%), dermatology (9.8%), and internal medicine (9.8%). Most HCPs reported working at a university hospital (62.3%); whereas 18.0% reported working in a public, nonuniversity hospital; and 13.1% reported working in a private clinic. Of the HCPs, 11.5% were 24–42 years of age; 45.9% were 43–54 years of age; 41.0% were 55–73 years of age; and 1.6% were > 73 years of age. HCP characteristics are reported in Table 2.

Perceived Impacts on Current and Future HAE Medical Care Due to the Pandemic

Most HCPs (95%) expected that their practice will be restricted, at least slightly, in the next 5 years because of COVID-19 restrictions. On average, a score of 3.0 of 5.0 on a scale from 1.0 to 5.0 was reported (1.0 being not at all restricted and 5.0 being extremely restricted), with the HCPs in group 2 expecting a higher impact versus the HCPs in group 1 (3.3 versus 2.7; $p = 0.01$) (Fig. 3). In addition, 78.3% of the HCPs expected that their treatment of patients with HAE will be permanently restricted and/or changed because of COVID-19; an average of 2.5 of 5 was reported, with the HCPs in group 2 expecting a higher impact versus group 1 (2.9 versus 2.2; $p = 0.01$, t-test, and $p = 0.02$, Wilcoxon rank sum test) (Fig. 3).

On average, on a scale from 1 to 5 (1 being not at all affected and 5 being extremely affected), the HCPs in group 2 believed that several aspects of HAE medical care will be more greatly affected in the next 5 years compared with the HCPs in group 1. Such aspects included the following: the organization of scheduled visits ($p = 0.03$, both tests); treatment distribution and dispensation ($p = 0.04$, t-test; and $p = 0.03$, Wilcoxon rank sum test); acute treatment drug choice ($p = 0.001$, both tests); prophylactic drug choice ($p = 0.003$, both tests); and the time to first diagnosis ($p = 0.01$, both tests) (Fig. 4). Overall, the HCPs in group 1 believed that organization of outpatient treatment is the most likely aspect of HAE care to be affected in the next 5 years by the pandemic (mean score, 2.8), and the HCPs in group 2 believed that the prophylactic drug choice is the most likely aspect of HAE care to be affected in the next 5 years (Fig. 4). In addition, most HCPs expect that the demand will increase for home supply of HAE treatments (60.7%) and self-administration training

Table 2 **Health-care provider characteristics**

	Group 1 (n = 37)	Group 2 (n = 24)	Total (N = 61)
Age range, n (%)			
24–42 years	5 (13.50)	2 (8.3)	7 (11.5)
43–54 years	16 (43.2)	12 (50.0)	28 (45.9)
55–73 years	15 (40.5)	10 (41.7)	25 (41)
>73 years	1 (2.7)	0	1 (1.6)
Country, n (%)			
Argentina	0	2 (8.3)	2 (3.3)
Australia	1 (2.7)	0	1 (1.6)
Austria	1 (2.7)	0	1 (1.6)
Bosnia and Herzegovina	0	1 (4.2)	1 (1.6)
Brazil	0	2 (8.3)	2 (3.3)
Bulgaria	1 (2.7)	0	1 (1.6)
China	0	1 (4.2)	1 (1.6)
Croatia	2 (5.4)	0	2 (3.3)
Czech Republic	1 (2.7)	0	1 (1.6)
Denmark	1 (2.7)	0	1 (1.6)
El Salvador	0	1 (4.2)	1 (1.6)
France	3 (8.1)	0	3 (4.9)
Georgia	0	1 (4.2)	1 (1.6)
Germany	3 (8.1)	0	3 (4.9)
Greece	2 (5.4)	0	2 (3.3)
Israel	3 (8.1)	0	3 (4.9)
Italy	2 (5.4)	0	2 (3.3)
Japan	1 (2.7)	0	1 (1.6)
Lebanon	0	1 (4.2)	1 (1.6)
Lithuania	1 (2.7)	0	1 (1.6)
Mexico	0	1 (4.2)	1 (1.6)
North Macedonia	0	5 (20.8)	5 (8.2)
Peru	0	2 (8.3)	2 (3.3)
Poland	1 (2.7)	0	1 (1.6)
Portugal	2 (5.4)	0	2 (3.3)
Romania	1 (2.7)	0	1 (1.6)
Serbia	0	4 (16.7)	4 (6.6)
Slovak Republic	1 (2.7)	0	1 (1.6)
Slovenia	1 (2.7)	0	1 (1.6)
Spain	1 (2.7)	0	1 (1.6)
Sweden	2 (5.4)	0	2 (3.3)
Switzerland	1 (2.7)	0	1 (1.6)
Turkey	0	2 (8.3)	2 (3.3)
United Kingdom	1 (2.7)	0	1 (1.6)
United States	4 (10.8)	0	4 (6.6)
Venezuela	0	1 (4.2)	1 (1.6)
Physician specialty n (%)			
Immunology	2 (5.4)	2 (8.3)	4 (6.6)
Clinical immunology	10 (27.0)	3 (12.5)	13 (21.3)
Dermatology	4 (10.8)	2 (8.3)	6 (9.8)
Internal medicine	4 (10.8)	2 (8.3)	6 (9.8)
Allergy	11 (29.7)	12 (50.0)	23 (37.7)
Gastroenterology	0	1 (4.2)	1 (1.64)
Other	6 (16.2)	2 (8.3)	8 (13.1)

Table 2 **Continued**

	Group 1 (n = 37)	Group 2 (n = 24)	Total (N = 61)
Practice type, n (%)			
Solo	0	0	0
Community hospital	0	2 (8.3)	2 (3.3)
Public hospital/center	6 (16.2)	5 (20.8)	11 (18.0)
University hospital	27 (73.0)	11 (45.8)	38 (62.3)
Private clinic	3 (8.1)	5 (20.8)	8 (13.1)
Other	1 (2.7)	1 (4.2)	2 (3.3)

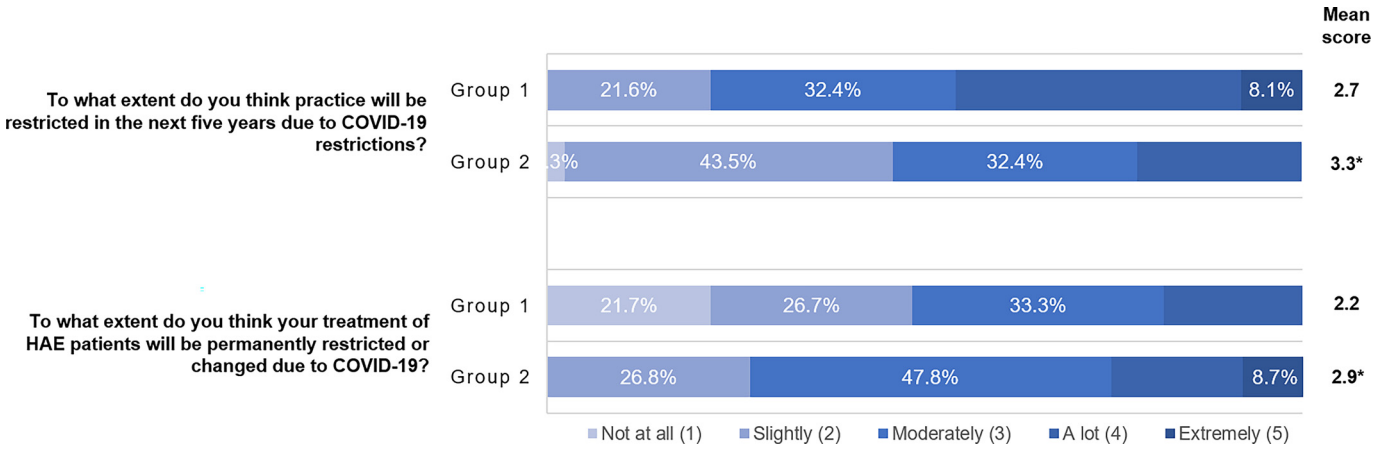

Figure 3. *HCP-perceived impact of the COVID-19 pandemic on HAE care and/or treatment. *p ≤ 0.05. HCP = Health-care professional; COVID-19 = coronavirus disease 2019; HAE = hereditary angioedema.*

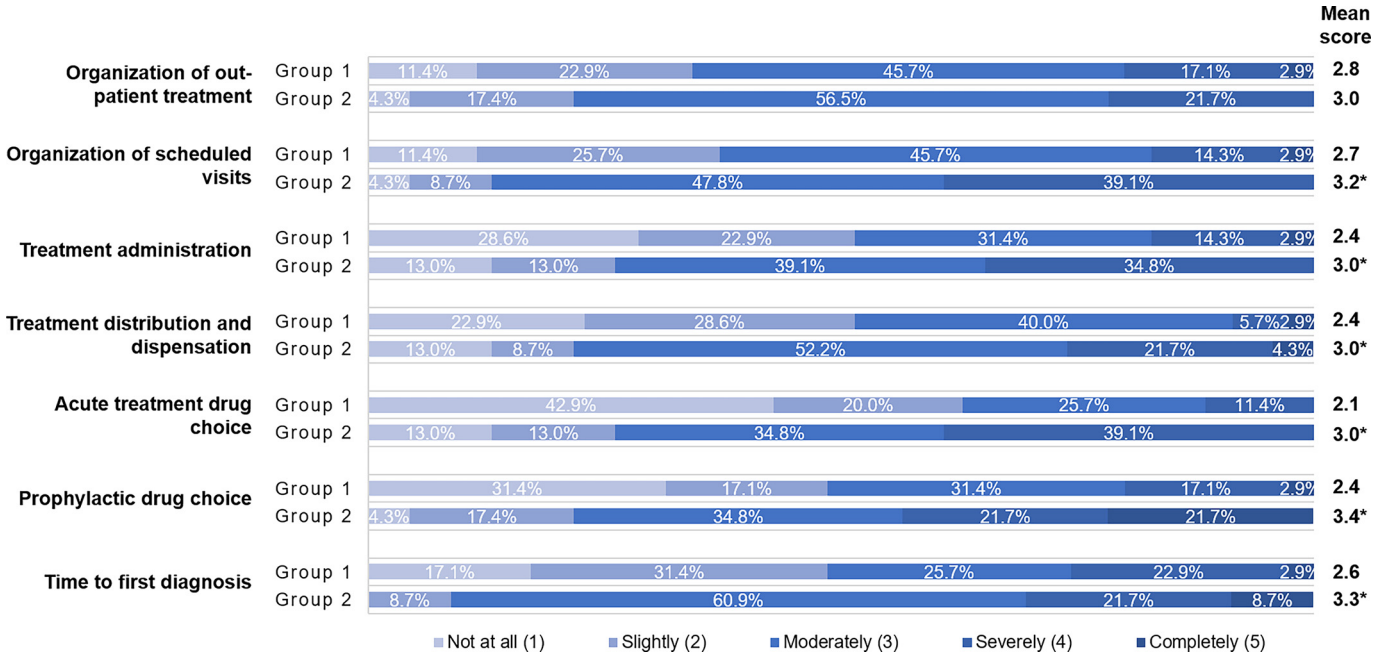

Figure 4. *HCP-perceived impact of the COVID-19 pandemic on various aspects of HAE-related care and/or treatment in the next 5 years. *p ≤ 0.05. HCP = Health-care professional; COVID-19 = coronavirus disease 2019; HAE = hereditary angioedema.*

(67.9%), and that the perceived importance of self-administration (80.4%) and subcutaneous (SC) administration (75.0%) will increase because of the pandemic. Despite these perceived effects, only 26.7% of the HCPs reported being dissatisfied with the range of services that they can offer to patients with HAE during the pandemic compared with what they could offer before the pandemic. An average score of 3.2 of 5 on a scale from 1 to 5 was reported (1 being very dissatisfied and 5 being very satisfied; no significant difference between the groups).

Satisfaction with Telehealth for HAE Management

Most of the HCPs (73.3%) agreed that face-to-face consultations for HAE management are important and reported an average score of 4.0 of 5 on a scale from 1 to 5 (1 being not important and 5 being very important; no significant difference between the groups). However, 78% of the HCPs rated remote care visits and/or consultations as a primary means of managing patients with HAE as acceptable, good, or very good, reported an average score of 3.2 of 5 on a scale from 1 to 5 (1 being very poor and 5 being very good; no significant difference between groups). In fact, half of the HCPs reported that they were likely to continue using telemedicine and/or remote visits as a means of managing patients with HAE in the post–COVID-19 era. An average score of 3.5 of 5 on a scale from 1 to 5 was reported (1 being highly unlikely and 5 being highly likely), with group 1 being more likely to continue telehealth and/or remote visits versus group 2 (3.8 versus 3.2; $p = 0.01$, both tests).

Unmet Needs

The HCPs were asked the following: "If you could give one piece of advice to colleagues regarding the treatment of HAE in the post–COVID-19 era, what would it be?" The HCPs could choose one of the following options (results are included in parentheses after each option): "Regularly check the status of your patients, even if they aren't asking for a consultation" (32.8%); "Educate patients to more accurately assess whether they do or do not need to see their HCP" (29.3%); "Help patients to clearly identify the symptoms of HAE through improved HCP-patient communications" (24.1%); "Improve response time when patients report symptoms that may appear ambiguous or unclear" (8.6%); and "Other" (5.2%).

COVID-19 Diagnoses

Approximately one-fifth of HCPs surveyed (20.7% [n = 12]) reported treating a patient with HAE who was diagnosed with COVID-19 (8 HCPs from group 1 and 4 HCPs from group 2). Eight of the patients reported having mild symptoms, whereas two patients were reported as having severe symptoms, which required intensive care (2 of the 12 patients did not have the severity reported). Both severe cases were reported by the HCPs from group 1 (United States) and were experienced by patients who received HAE prophylaxis at the time of their diagnosis. Neither experienced a change in frequency or severity of HAE attacks during their infection. Overall, three HCPs reported a change in HAE attack frequency and four reported a change in HAE attack severity in association with a COVID-19 diagnosis.

DISCUSSION

To our knowledge, this was the first global report that described the effects of the COVID-19 pandemic on future HAE medical care from the patients' and HCPs' perspectives. This study found that most of the patients and the HCPs agreed that the pandemic had limited the availability of HAE medical care, and they expected the restrictions to continue far beyond the pandemic, possibly for >5 years. This sentiment was expressed by the respondents from both country groups; however, it was more frequently expressed by the patients and the HCPs from group 2, specifically with regard to challenges with prophylactic medication access. In addition, most of the HCPs expected that the demand for self-administered therapies will increase because of the pandemic.

The HAE armamentarium includes several on-demand and prophylactic therapies that can be safely administered at home by the patient, *e.g.*, subcutaneous treatments such as the plasma-derived C1-INH concentrate SC-C1-INH and the plasma kallikrein inhibitor lanadelumab as well as oral options, such as the plasma kallikrein inhibitor berotralstat and anabolic androgens (as a second-line option).[12,14,19–21] However, access issues may limit the availability of these medications for patients in non–high-income countries or in countries with restrictive health-care payer systems.[14,15]

In addition, income inequalities can also arise within countries, which results in health-care disparities among individuals of the same country, with lower-income citizens having less access to medical treatments and services than their higher income counterparts have.[22–24] It is likely that patients with low socioeconomic status will have less access to newer medications, regardless of the country in which they reside. The pandemic has likely increased this access disparity, which intensified concerns with regard to the availability of necessary medications for patients with HAE of a low socioeconomic status. Easier access to HAE medications may be even more important for patients during the pandemic because many patients have experienced an increase in HAE attack rates since

the pandemic began, presumably because of increased anxiety and psychological stress.[25,26]

Most patients and HCPs agreed that face-to-face consultations for HAE management are important; however, they also reported that telehealth and/or remote consultations are still useful. Of interest, patients from high-income countries reported that face-to-face consultations are of lower importance and telehealth and/or remote consultations are more useful compared with patients from non–high-income countries. In addition, the HCPs from the high-income countries reported being more likely to continue telehealth consultations in the post–COVID-19 era. The difference in telehealth satisfaction between the country groups may be explained by examining the differences in availability of advanced technologic infrastructures that can support successful telehealth platforms, which exist more commonly in high-income countries.[8]

A total of seven patient respondents reported a previous diagnosis of COVID-19, and 12 HCPs reported treating patients with HAE who had been previously diagnosed with COVID-19. Limited research is available with regard to how a COVID-19 diagnosis might affect patients with HAE. Because of the overlap of pathophysiologic mechanisms (bradykinin influx) between HAE and COVID-19 symptoms,[27] it has been hypothesized that COVID-19 may worsen a patient's HAE symptoms, or *vice versa*, and that prophylactic HAE treatments may be protective against severe COVID-19 symptoms.[28–30] Results of a small Brazilian study ($N = 13$) and a larger study conducted in Turkey ($N = 67$) suggest that patients with HAE who develop COVID-19 are not at an increased risk for severe symptoms of either ailment.[31,32]

Both severe cases in our study (10.5%) were reported by the HCPs from group 1 (United States), which occurred at a similar rate to the average U.S. population (range, 4.9%–11.5%).[33] Both patients were receiving HAE prophylaxis at the time of their COVID-19 diagnosis. In addition, some HCPs reported that their patients experienced an increase in severity or frequency of HAE symptoms due to COVID-19; however, it is unclear if those patients were receiving prophylactic therapy before their COVID-19 diagnosis. Our sample sizes were small, thus additional studies with larger patient samples are necessary to understand the risk of patients with HAE and COVID-19 developing severe symptoms of either disease.

LIMITATIONS

This study had several limitations, including a small global patient and HCP sample size with an unequal distribution of respondents across countries. In addition, some countries had few patient responders who may not be an accurate reflection of the entire patient population and could lead to biased results. Patient characteristics were not matched across country groups and individual incomes were not assessed; thus, some patients from high-income countries may have had a personal low-income status and *vice versa*. In addition, countries may also have unique challenges with regard to the specific health-care system and infrastructure in place that is unrelated to the average national income and may affect patient and physician perspectives. Thus, the patients in two different high-income (or low-income) countries may not share similar health-care experiences.

Links that are provided on the personal social media accounts of one of us (V.G-P.) may have contributed to the skewed country-level responses. In addition, there was no method of validation to confirm that only patients and HCPs responded to the survey, although screener questions were included to select target participants. Survey respondents were ≥ 18 years of age, therefore, did not represent children diagnosed with HAE who may have a different experience from adults. Certain questions were developed with the assumption that the effects of the pandemic would be negative on patients and physicians, thus potentially biasing responses. The assumptions were made based on the extensive clinical experience of the authors in treating patients with HAE.

CONCLUSION

This report highlights the need to define sustainable medical standards of HAE care across countries and ensures additional medical, technologic, and economic support for non–high-income countries so that they can achieve international standards. Safe, effective, and easy-to-use medications should be available to patients who need them, regardless of their country and socioeconomic status. The use of telehealth practices has increased since the pandemic began, and both the patients and the HCPs reported a high level of satisfaction with current telehealth services, although respondents in country group 2 reported lower overall satisfaction compared with respondents in country group 1. Disparities in medical care and the technologic infrastructure are common challenges for non–high-income countries, which can be exacerbated during a global crisis such as a pandemic; therefore, new tools and the global infrastructure should be developed to provide this type of support during similar events in the future.

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